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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,444	01/31/2005	Jean Guy Gilles	50304/059001	4465

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CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER	
SZPERKA, MICHAEL EDWARD	
ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
12/24/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/523,444	GILLES ET AL.	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,18-20,22,24-26,28 and 31-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1, 18-20, 22, 24-26, and 31-41* is/are allowed.

6)☒ Claim(s) *28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 6, 2008 has been entered.

Claims 2-17, 21, 23, 27, 29, and 30 have been canceled.
Claims 1, 20, 22, 25, 34, 35 have been amended.
Claims 37-41 have been added.
Claims 1, 18-20, 22, and 24-26, 28, 31-41 are pending in the instant application.

2. Applicant's claim amendments received October 6, 2008 have overcome all prior grounds of rejection.

3. Claims 1, 18-20, 22, 24-26, 32-37, 40, and 41 are directed to an allowable product. Pursuant to the procedures set forth in MPEP § 821.04(B), claims 28, 31, 38, and 39, directed to the process of making or using an allowable product, previously withdrawn from consideration as a result of a restriction requirement, are hereby rejoined and fully examined for patentability under 37 CFR 1.104.

Because all claims previously withdrawn from consideration under 37 CFR 1.142 have been rejoined, **the restriction requirement as set forth in the Office action mailed on May 24, 2007 is hereby withdrawn**. In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may

be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 28 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating uncontrolled bleeding in a patient with FVIII inhibitory antibodies that bind the C2 domain of FVIII, does not reasonably provide enablement for methods of treatment for all patients comprising FVIII inhibitory antibodies generically. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicant has claimed a method of treating individuals suffering from uncontrolled bleeding by administering an anti-idiotypic antibody or antigen binding fragment thereof. The patients to be treated by the claimed method are further characterized in that they comprise FVIII inhibitory antibodies.

The specification discloses that BO2C11 is an inhibitory antibody obtained from a hemophilia patient that was used as an antigen to generate an anti-idiotypic response, with the hope that the elicited anti-idiotypic antibodies could be used in therapeutic methods. The idiotype of an antibody is the unique structure formed in an antibody that provides antigen specificity (i.e. CDR loops and nearby framework residues), and it has been observed in the art that antibodies which bind antibody idiotypes often resemble the initial target antigen (i.e. antibody A binds antigen X; anti-idiotypic antibody that binds A comprises an idiotype that structurally mimics the three-dimensional surface of

X). Applicants have generated an anti-idiotypic antibody that binds BO2C11 that they have named 14C12, and have indicated that the idiotype of 14C12 mimics FVIII and thus competes with FVIII for binding to inhibitory antibodies. As such, applicants assert that 14C12 can be administered in a manner such that complexes preferentially form between inhibitor and 14C12, leaving FVIII unbound by inhibitor and thus able to participate in thrombus formation. The antibody used to generate the anti-idiotype antibody binds to the C2 domain of FVIII, and thus the anti-idiotypic antibody that is administered as part of the claimed method comprises a structure that mimics that of the C2 domain of FVIII. Note that all SEQ ID numbers recited in the instant claims are subsequences of the full length heavy and light antibody chains of 14C12

Autoantibody responses directed against FVIII are typically polyclonal, but typically only antibodies directed against the A2, A3, and C2 domains of FVIII are observed to inhibit coagulation activity, and thus only antibodies to these domains are typically observed to be "inhibitors" (see particularly page 3 of the instant specification and Gilles et al., Thrombosis and Haemostasis 1997, 78:641-646, entire document but especially Figure 1). These domains are spaced widely enough apart in the structure of FVIII that inhibitors that bind one domain do not compete with inhibitors that bind other domains (Shima et al., Thrombosis and Haemostasis, 1993, 69:240-246, see entire document, particularly Figure 6 and the bottom of the left column of page 244). Further, it is known that patients comprising inhibitory antibodies do not necessarily comprise inhibitors that bind to the C2 domain, since antibodies that bind other domains can also act as inhibitors (Muhle et al., Thrombosis and Haemostasis, 2004, 91:619-625, see entire document, particularly Patient I in Table 1). As discussed above, the therapeutic method is based upon the administered antibody acting as a structural mimic of FVIII such that inhibitory antibodies bind to the administered antibody rather than to FVIII. Thus, the patient will only receive benefit if the patient comprises inhibitory antibodies that bind the C2 domain of FVIII. Patients lacking inhibitors directed toward the C2 domain of FVIII would not receive any benefit by the instantly recited method, yet such patients are not excluded from the instant claimed method.

Therefore, based upon the teachings and guidance of the instant specification and the teachings of the art, a skilled artisan would be unable to practice the full scope of the instant claimed invention as currently recited.

6. Claims 1, 18-20, 22, 24-26, 31-41 are allowable.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is (571)272-2934. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michael Szperka, Ph.D.
Primary Examiner
Art Unit 1644

/Michael Szperka/
Primary Examiner, Art Unit 1644